CASE REPORT

Left ventricular noncompaction diagnosed following Graves' disease

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ABSTRACT

Isolated left ventricular noncompaction (LVNC) is a rare genetic cardiomyopathy. Clinical manifestations are variable; patients may present with heart failure symptoms, arrhythmias, and systemic thromboembolism. However, it can also be asymptomatic. When asymptomatic, LVNC can manifest later in life after the onset of another unrelated condition. We report a case of LVNC which was diagnosed following a hyperthyroid state secondary to Graves' disease. The association of LVNC with other noncardiac abnormalities including neurological, hematological, and endocrine abnormalities including hypothyroidism has been described in isolated case reports before. To the best of our knowledge, this is the first reported case of LVNC diagnosed following exacerbation in contractile dysfunction triggered by Graves' disease.

Key words: Echocardiography, Graves' disease, noncompaction cardiomyopathy

INTRODUCTION

Left ventricular noncompaction (LVNC) is a rare genetic cardiomyopathy.[1] Clinical manifestations are variable, and patients may present with heart failure symptoms, arrhythmias, and systemic thromboembolism. However, it can also be asymptomatic.[2] Various congenital heart disorders and neuromuscular disorders have been associated with LVNC.[3-5]

CASE REPORT

A 26-year-old African American female with no significant medical history presented with shortness of breath, palpitation, and lower extremity swelling for 1 month. She also reported orthopnea, markedly diminished exercise capacity, and heat intolerance. The patient did not have any family history of cardiac or autoimmune diseases. Initial vital signs showed blood pressure of 120/90 mmHg, heart rate of 134 beats/min, respiratory rate of 20 breaths/min, temperature of 37.6°C, and oxygen saturation of 98% breathing ambient air. Physical examination was significant for jugular venous distension and enlarged thyroid gland. Cardiac examination showed tachycardia with normal heart sounds without murmurs or rubs. Lung examination revealed bilateral lower lobe rales. Examination of the extremities revealed bilateral edema. Initial laboratory results showed elevated brain natriuretic peptide of 623 pg/ml, elevated T4 (4.49 ng/dl), and low thyroid stimulating hormone (<0.01 uIU/ml). Complete blood count and chemistry tests were within normal limits. Twelve leads electrocardiogram showed only sinus tachycardia. Further workup revealed an elevated antithyroglobulin antibody (290 IU/ml) and elevated thyroid stimulating immunoglobulin (261%); thyroid ultrasound showed a heterogeneous enlarged thyroid gland with thick isthmus and increased vascularity which confirmed the diagnosis of Graves' disease and the patient was started on methimazole and propranolol.

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Echocardiogram and further contrast echocardiography revealed severely reduced global LV function with an estimated ejection fraction (EF) of 25–30%, mild tricuspid regurgitation; the right ventricular was normal with estimated systolic pressure of 49 mmHg indicating mild pulmonary hypertension**.** In addition, hypertrabeculation in the inferolateral walls suggesting noncompacted heart muscles was also seen [Figure 1a and b].

Cardiac magnetic resonance imaging was also done and revealed enlargement of the four heart chambers, severe biventricular dysfunction with an EF of 30%, and increased noncompacted myocardium (NC) to compacted myocardium (C) ratio at the distal lateral wall and apex which confirmed diagnosis of LVNC with a ratio of 3.5, with no evidence of delayed myocardial enhancement to suggest myocarditis [Figure 2a and b].

The patient was medically treated for systolic heart failure with diuretic, beta-blockers, angiotensin-converting enzyme inhibitors, and spironolactone. She also received family and genetic counseling. During her stay, she had runs of nonsustained ventricular tachycardia (VT) with a high premature ventricular contraction burden (>24%). The plan was to treat the thyroid disease and medically optimize the patient for 3 months and then reevaluate the patient clinically. The patient was discharged home with a wearable cardioverter defibrillator, and she was also scheduled for follow-up to check thyroid function and echocardiogram to reassess the EF. After 3 months, her thyroid function was within normal limits and a follow-up echocardiogram revealed that the EF has improved to 40–45%, with the same hypertrabeculation in the inferolateral walls.

DISCUSSION

LVNC is a rare cardiomyopathy that is classified as a genetic cardiomyopathy by the American Heart Association.[1] It has an estimated prevalence of 0.014–0.7% among patients undergoing echocardiography and 3–4% among heart failure patients,[2,3] with higher incidence noted in the African American community.[4] LVNC is characterized by modification of the LV wall into an outer compact layer and an inner noncompacted layer consisting of deep intratrabecular recesses and prominent trabeculations resulting in clinical manifestations of dilated cardiomyopathy.

Pathogenesis

The congenital theory of pathogenesis of LVNC postulates that LVNC results from arrest of the compaction process during the 2nd month of embryological development. The normal process of compaction of the loose meshwork of myocardium which occurs during the 5th and 8th week of gestation is arrested due to unknown mechanism at various stages, resulting in varying degree of noncompaction.[6] The other proposed mechanism for development of LVNC includes acquired microcirculatory dysfunction leading to microinfarcts and resultant hypertrabeculation.[7] In addition, patients with chronically elevated preload or afterloads such as valvular heart disease,[8] sickle cell disease,[9] chronic renal failure, and high-performance athletes[4] have a high prevalence of trabeculations and may also fulfill criteria for LVNC.

LVNC may occur in isolation or may be associated with other cardiac abnormalities such as arrhythmogenic right ventricular dysplasia, hypertrophic, restrictive, or dilated cardiomyopathy, congenital heart disease, and complex syndromes affecting multiple organ systems.[10,11] LVNC has also been reported in association with Ebstein's anomaly and bicuspid aortic valve. There are reports on association of LVNC with other noncardiac abnormalities including neurological, facial, and hematological. In addition, endocrine abnormalities including hypothyroidism and dermatological and skeletal anomalies have also been described in isolated case reports.[5,12]

In patients with hyperthyroidism, heart failure may occur in the absence of underlying heart disease. Most patients with hyperthyroidism are in a high cardiac output state without heart failure symptoms.[13] However, reduced LV contractile reserve may impair the ability to increase the cardiac output

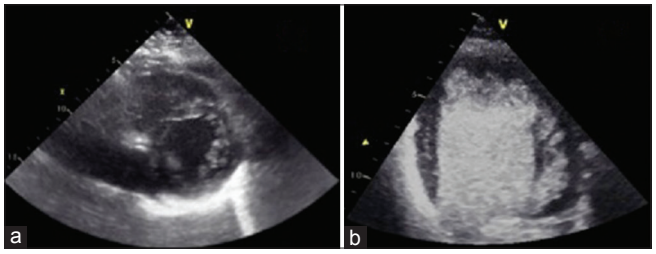

Figure 1: (a) Parasternal short axis view echocardiography showing noncompacted myocardium. (b) Contrast echocardiography demonstration hypertrabeculation

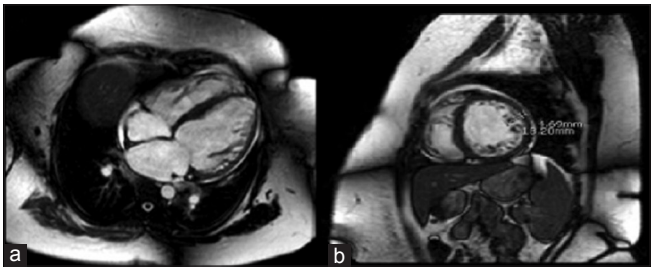

Figure 2: (a) Long axis cardiac magnetic resonance imaging showing hypertrabeculation. (b) Short axis view cardiac magnetic resonance imaging showing, noncompacted and compacted myocardial layers

to match the increase of peripheral demand. In our case, we think that Graves' disease-induced hyperthyroidism led to a remarkable increase in preload and heart rate resulting in precipitation of heart failure.[13] To the best of our knowledge, this is the first reported case of LVNC diagnosed following exacerbation in contractile dysfunction triggered by Graves' disease.

Clinical features

LVNC shows a male predominance with median age of presentation ranging from 4th to 5th decades. Familial occurrence rates of 18–50% have been reported in different case series.[2-5,14] Heart failure remains the most common initial presentation;[5] arrhythmias including atrial fibrillation (AF),[2,3,5] VT, and Wolff–Parkinson–White syndrome are also common.[5,14] Ventricular thrombi have been reported in 9–25% of patients with LVNC with a high incidence of systemic embolism (21–38%).[2,3] A systematic review included five studies with a total of 241 adults with LVNC with a mean of 39 months follow-up and showed an annual cardiovascular death rate of 4%; the overall mortality rate was 14% during 39 months; nearly half of deaths were from sudden cardiac arrest.[15] Another case series have also shown better prognosis in VT individuals who are asymptomatic at diagnosis.[16] Prognostic scoring systems are not available considering the rarity of disease. However, in a German registry, the presence of AF, reduced LV function, and LV dilatation and the presence of mitral regurgitation had a significant impact on the prognosis of the enrolled patients.[17] End-systolic noncompacted to compacted ratio of >2 was associated with worse clinical outcomes in another study.[18]

Diagnosis

Two-dimensional echocardiography is the most frequently used imaging modality, with various criteria proposed by different authors.[2,5] The criteria proposed by Jenni *et al*.[19] are the most commonly used in clinical practice and include noncompacted to compacted myocardium ratio of >2:1 at end-systole in the parasternal short-axis view, absence of other cardiac abnormalities, and color Doppler flow within intertrabecular spaces. However, there are no gold standard criteria for diagnosis of LVNC. Contrast echocardiography can aid in diagnosis, especially in patients with poor acoustic windows by better definition of endocardial borders and identification of mural thrombi.[20,21]

Cardiovascular magnetic resonance (CMR) imaging can help in diagnosis of LVNC by better visualization of "two-layered" myocardium with a ratio of noncompacted to compacted myocardium >2.3 in diastole (sensitivity 86%, specificity 99%)[22] and by ruling out other related cardiomyopathies such as dilated cardiomyopathy, hypertensive heart disease, apical hypertrophic cardiomyopathy, infiltrative cardiomyopathy, and eosinophilic endomyocardial disease. Jacquier *et al*.[23] used LV trabecular mass of >20% as a cutoff for diagnosis of LVNC and reported sensitivity of 93.7% based on the above-mentioned Jenni criteria.

Management

There are no specific guidelines for management of LVNC. Management consists largely of guideline-directed medical therapy for heart failure. Indication for oral anticoagulation in LVNC includes AF and documented LV thrombus. However, the use of anticoagulation in patients with LVNC and low or preserved EF without evidence of AF or LV thrombus remains controversial as no strong evidence exists for or against it. There is lack of data on use of implantable cardioverter defibrillator (ICD) for LVNC. A small case series reported 42% appropriate ICD therapy in patients who had ICD and a high rate of supraventricular tachyarrhythmia (66%).[24] Another small study showed that ICD with biventricular pacing resulted in improved the New York Heart Association functional class in LVNC patients with severely reduced LVEF and evidence of dyssynchrony.[25] This study also showed appropriate device therapy in 38% of patients with normal EF, thus indicating that device therapy may be independent of EF.

CONCLUSION

LVNC is a rare cardiomyopathy that can rarely be asymptomatic and manifest later in life following other unrelated conditions that lead to exacerbation in contractile dysfunction such as Graves' disease. Echocardiography is the standard tool for diagnosis, and CMR is very useful to confirm or rule out this disease.

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Conflicts of interest

There are no conflicts of interest.

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